

REMARKS

Prosecution has been reopened by the Examiner (see paragraph 2 of the Office Action). This reply addresses the rejection in the outstanding Office Action. Any previous rejection not discussed in the Office Action has been withdrawn, such as that indicated in paragraph 5 of the Office Action.

Status of the Claims

Claims 14-17, 19, 20 and 22-23 are pending in this application. No claims are presently canceled, added or amended. Thus, a listing of the claims is not necessary.

In view of the following remarks, Applicant respectfully requests that the Examiner withdraw the only rejection and allow the currently pending claims.

Issues Under 35 U.S.C. § 103(a)

Claims 14-17, 19, 20, 22 and 23 stand rejected as being unpatentable over Thorns '241 (U.S. Patent No. 5,510,241) in view of Zawistowski '694 (U.S. Patent No. 5,807,694). Applicant respectfully traverses, and reconsideration and withdrawal of this rejection are respectfully requested.

Essentially, the Examiner relies on Thorns '241 in the same manner as in the previous rejection, while referring Applicant to various parts of the primary reference. Also, in the current Office Action the Examiner further relies on the secondary reference of Zawistowski '694 which is asserted to be disclosing a method of detecting Salmonella from eggs within a time period of 6 hours. Regarding this disclosure in Sawistowski '694, the Examiner refers Applicant to column 5, lines 15-65 and column 7, lines 1-7 of the secondary reference (see

the Office Action at page 3, lines 15-16). This is followed by the conclusion of obviousness (at page 3, lines 17+ of the Office Action). Applicants respectfully traverse.

Applicants respectfully submit that Zawistowski '694 has been misinterpreted, and that a *prima facie* case of obviousness has not been established. One of ordinary skill in the art would not combine the cited references, and thus the instant rejection is improper.

Distinctions over the Combination of Thorns '241 and Zawistowski '694: Lack of Disclosure of All Claimed Features

The Examiner relies on the teachings of Thorns '241 for allegedly disclosing a method for detecting the presence of *Salmonella* species expressing fimbrial antigens, which have been grown on a select medium (referring to the Abstract, Title and claims of the reference). The Examiner further refers Applicant to parts of columns 5, 6, 7, 11 and 26-28 in asserting that the primary reference of Thorns '241 discloses most of the instantly claimed features. The Examiner admits that Thorns '241 fails to disclose or teach a rapid method of detection where the detection assay is effective within 3 to 10 hours from the onset of cultivation (page 3, line 14 of the Office action). Therefore, the Examiner relies on the cited secondary reference of Zawistoski '694 for the missing disclosure in Thorns '241.

However, Applicant respectfully submits that the combination of Thorns '241 and Zawistoski '694 fails to disclose or suggest all of the claimed elements of the present invention. In the Office Action at page 3, lines 15-16, the Examiner asserts that the secondary reference of Zawistowski '694 discloses detection of *Salmonella* from eggs within a time period of 6 hours (referring to column 5, lines 15-65 and column 7, lines 1-7), and thus accounting for the deficiencies of Thorns '241. This is technically incorrect.

A closer review of the cited Zawistowski '694 reference shows that Zawistowski '694 fails to disclose a shortened cultivation step as claimed in the present invention. Applicant notes that an analysis under 35 U.S.C. § 103(a) requires a determination of the scope and content of the prior art, *Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966). Zawistowski '694 instead discloses a 6-hour pre-enrichment incubation step and an 18-hour enrichment incubation step and not what is asserted in the outstanding Office Action. More specifically, the asserted disclosure at column 5 of Zawistowski '694 is a prior incubation step. At column 5, line 676 to column 6, line 2, it is stated, "...and the presence of the antigen is detected by any convenient method for detecting formed antibody-antigen complexes, . . .". Incubation time is not specified therein, but later at column 6, lines 28-30, Zawistowski '241 discloses that "Combined with the prior incubation step, in its optimum form, the assay requires less than 24 hours ...".

Further, at column 7, line 3, the secondary reference discloses that the preincubation step lasts "up to six hours". However, on lines 6-7 in the same column, the secondary reference further states that "The mixture is then incubated for an additional 18 hours at about 37°C". Consequently, the comments at page 3 of the Office Action contradict the actual disclosure in Zawistowski '694.

Thus, the Examiner has failed to establish a *prima facie* case of obviousness since all of the steps of the claimed method are neither disclosed nor suggested by the combination of Thorns '241 and Zawistowski '694. U.S. case law squarely holds that a proper obviousness inquiry requires consideration of three factors: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) whether or not the prior art would have taught, motivated, or suggested to those of ordinary skill in the art that they

should make the claimed invention (or practice the invention in case of a claimed method or process); and (3) whether the prior art establishes that in making the claimed invention (or practicing the invention in case of a claimed method or process), there would have been a reasonable expectation of success. *See In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Here, Zawistowski '694 does not account for the deficiencies of Thorns '241, and this rejection has been overcome since not all requirements for a *prima facie* case of obviousness have been satisfied (e.g., disclosure of all instantly claimed features).

Applicant also submits that neither Thorns '241 nor Zawistoski '694 suggest modifying the method that is taught in Thorns '241 with the teachings in Zawistoski '694. In other words, the requisite motivation and/or reasonable expectation of success are lacking as well (as discussed in more detail in the next section below).

The Improper Combination of Thorns '241 with Zawistowski '694: Lack of Motivation and Reasonable Expectation of Success

The requisite level of motivation for establishing a *prima facie* case of obviousness has not been met.

With regard to the asserted combination, Thorns '241 discusses fimbriae, whereas Zawistowski '694 is directed to lipopolysaccharide antigens (LPS). However, the synthesis and regulation of the fimbriae and the lipopolysaccharide antigens (LPS) are two distinct phenomena, which take place independently of each other. In other words, one of ordinary skill in the art would not be motivated in combining Thorns '241 with Zawistowski '694 in order to achieve the presently claimed invention.

More specifically, the fimbrial antigens of Thorns '241 are proteins or their peptide derivatives which are originating from the fimbriae that are cellular appendices. On the contrary, the LPS of Zawistowski '694 is an essential part of the outer compartment of the lipid bilayer membrane (the outer membrane) consisting of both lipid and polysaccharide parts, but not of any proteinaceous components. The outer membrane is surrounding the Gram-negative bacterial cells in all circumstances, whereas the fimbrial expression is more variable. In fact, it is possible that these appendices are not expressed at all, which condition is not preventing the normal life cycle of the cells.

Further, Applicant respectfully refers the Examiner to the literature by Neidhardt et al. (Niedhardt, F.C., Ingraham, J.L. and Schaechter, M., *Physiology of the Bacterial Cell. A Molecular Approach*, Sinauer Associates, Inc., Mass. (1990)), which states regarding the outer membrane: "Its outer leaflet, on the other hand, has a unique constituent in the place of phospholipids. This component is the bacterial LIPOPOLYSACCHARIDE, or LPS, a complex molecule not found elsewhere in nature." Further, regarding fimbriae, the same Niedhardt reference states: "Pili [singular: pilus, or "hair"] are a second type of protein structure projecting beyond the bacterial surface (Eisenstein, 1987). They are also known as fimbriae. Pili are organelles of attachment to surfaces and exhibit remarkable specificity." On the basis of the scientific quotations above, it is clear that these different cell structures have completely different tasks, characteristics and constitution. Further, the research of each has evolved in separate ways with hardly any similarities. Thus, it was not by any means evident to the skilled artisan to apply any method used for the LPS studies for any analysis or detection of fimbrial antigens, which were by the time of invention believed to be in

prepositional to the cell number in general. Thorns '241 has been improperly combined with Zawistowski. '694.

Therefore, one of ordinary skill in the art would recognize and understand that the synthesis and regulation of the fimbriae is scientifically a distinct phenomena from that of LPS. The two methods disclosed in Thorns '241 and Zawistowski '694 take place independently of each other. Therefore, Applicant respectfully submits that the skilled artisan would not combine the two cited references. Further, Applicant respectfully requests the Examiner to reconsider the arguments in the Office Action taking these scientific facts (e.g., differences in regulating fimbriae versus LPS) into account, wherein the skilled artisan would not combine the methods. Applicant further submits that findings related to the synthesis of the outer membrane or the expression of its components or their use for the detection purposes do not give any hints with respect to the fimbrial biosynthesis or the expression of the fimbrial antigens or their use for diagnostic purposes whatsoever. Consequently, Applicant respectfully submits that the requisite motivation is lacking. *In re Vaeck*.

Further, because Zawistowski '694 is directed to a method for the detection of the lipopolysaccharide antigens, which is contrast to Thorns '241, Applicant submits that the references are not in an analogous art with each other. When relying on a cited reference(s), where the cited reference(s) is used to reject the applicant's invention, that reference(s) "must either be in the field of the applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned". *In re Oetiker*, 24 USPQ2d 1443 (Fed. Cir. 1992) (24 USPQ2d at 1445; citing *In re Deminski*, 230 USPQ 313, 315 (Fed. Cir. 1986). That is not the case here given how the methods are technically different and are independent of each other.

Further, it is not clear as to why one of ordinary skill in the art would be motivated in combining a reference like Thorns '241 with a reference like Zawistowski '694 when the present invention is directed to a method of detecting enteric bacteria having fimbria. Zawistowski '694 is not directed to such a method as claimed, but is instead directed to detecting lipopolysaccharides. Applicant notes that if a proposal for modifying the cited reference in an effort to attain the claimed invention causes the reference to become inoperable or destroys its intended function, then the requisite motivation to make the modification would not have existed. *See In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984) (Federal Circuit stating that modifying the French apparatus as the Board suggested would render the apparatus inoperable for its intended purpose); *In re Fritch*, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992); *see also In re Ratti*, 123 USPQ 349, 352 (CCPA 1959). That is the case here because achieving the present invention would destroy the intended purpose of the Zawistowski '694 reference directed to the method of analyzing LPS.

Thus, based on the above, the requisite motivation is lacking. Reconsideration and withdrawal of this rejection are respectfully requested.

The Improper Combination of Thorns '241 with Zawistowski '694: Lack of Reasonable Expectation of Success

Further, the requisite reasonable expectation of success for establishing a *prima facie* case of obviousness has not been met.

Applicants note that the expression of fimbrial antigens within a time period of 3 to 10 hours is unpredictable in the light of the previous state of art, wherein even Thorns '241, as well as other references, disclose and teach a much longer time period to be needed for the

detection of these fimbrial antigens. Thus, Applicant submits that at the time of the present invention was made, no one had investigated the fimbrial expression during the very first hours of the population growth, because it was wholly not expected to attain or achieve a clear detection or enough antigenic material from relatively sparse populations from cultures, which just had been inoculated. In other words, the achievements of the present invention are unexpected given the state of the art.

In order to give further background from theoretical studies on the detection of bacteria on the basis of their fimbrial structures, Applicant previously submitted a manuscript which was a part of an academic dissertation (E.Hakalehto, "Characterization of *Pectinatus cerevisiiphilus* and *P.frisingiensis* Surface Components. Use of Synthetic Peptides in the Detection of Some Gram-negative Bacteria," University of Kuopio Publications, C. *Natural and Environmental Sciences* , Vol.112 (2000) (see "Exhibit C" with the Reply of October 8, 2003). In this previously submitted thesis, the same finding was clearly indicated as in the earlier priority application to this application: the amount of detectable fimbrial antigens surprisingly peaked only after a few hours of cultivation, in the very beginning of the exponential growth phase surprisingly regardless of the cell number. This finding was relatively revolutionary and is against any rational thinking of the skilled artisan, who would suppose that these parameters would logically positively correlate, which is the case with respect to the LPS antigens. Thus, Applicant submits that one of ordinary skill in the art would not have the reasonable expectation of success of achieving the present invention, even based on the disclosure in Thorns '241 and Zawistowski '694, since the expectations of the state of the art are contrary to the achievements of the present invention.

Applicant further submits that “Obviousness requires one of ordinary skill in the art have a reasonable expectation of success as to the invention—‘obvious to try’ and ‘absolute predictability’ are incorrect standards.” *Velandier v. Garner*, 68, USPQ2d 1769, 1784 (Fed. Cir. 2003) (citing *In re O’Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673 (Fed. Cir. 1988)). Here, an “obvious to try” rationale is being used to form the instant rejection given the comments in the Office Action at page 3, second to last line to page 4, line 2. Thus, the requisite reasonable expectation of success to establish a *prima facie* case of obviousness has not been satisfied.

Based on the above, the requisite reasonable expectation of success is lacking. *In re Vaeck*. Reconsideration and withdrawal of this rejection are respectfully requested.

Initial Burden by Examiner Has Not Been Met; Impermissible Level of Hindsight Reconstruction Has Been Applied

The Examiner has not met the initial burden of providing the proper suggestion of the desirability of doing what the instant inventor has done. Further, the Examiner states in the paragraph bridging pages 3-4 of the Office Action that it would be *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of screening taught by Zawistoski ‘694 and the method taught by Thorns ‘241 “to obtain the instant disclosure”. The Examiner further states that the motivation for making the combination is that rapid screening methods for bacteria, such as *Salmonella*, are needed. However, no evidence to support the Examiner’s statement has been provided. The Examiner also states that one would be motivated to develop a better method with a

shortened cultivation period for detecting bacteria that are major causes of food-borne illnesses. Again, no evidence of such motivation and/or reasonable expectation of success is provided. Thus, the Examiner has not met the initial burden of providing the proper suggestion of the desirability of doing what the instant inventor has done. *See Ex parte Clapp*, 227 USPQ 972, 973 (BPAI 1985); M.P.E.P. § 2142. No evidence has been provided by the Examiner regarding such means of combining the two cited references.

Further, regarding the Examiner's conclusion of obviousness in combining Thorns '241 with Zawitoski '694 (in the paragraph bridging pages 3-4 of the Office Action), the Examiner considers the technical problem as being the need for rapid screening (see page 3, lines 2-3 from the bottom of the page of the Office Action). The Examiner also cites shortening the cultivation period as a means of motivation and/or reasonable expectation of success. However, it is unreasonable to phrase the problems in these terms since it clear that the Examiner is reading Applicant's specification at page 2, lines 13-21. Applicant notes that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicant's disclosure. *See In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). That teaching or suggestion has not been found in the cited references, but instead in Applicant's specification. Applicants note that even the primary reference Thorns '241 discloses a much longer time period to be needed for the detection of the fimbrial antigens, and Zawistowski '694 is not even directed to detecting fimbrial antigens. In addition, considering the problem to be solved in the Examiner's terms implicitly includes a direction to the solution to the problem. This itself is unreasonable because the cited references ought to be considered without the benefit of

hindsight reconstruction. *See* M.P.E.P. § 2141 (“the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention”).

In this regard, the only way to achieve the present invention is to read the present specification, review what is being claimed, and using substantial hindsight reconstruction by combining reference A (Thorns ‘241) with reference B (Zawistowski ‘694). However, Applicant respectfully refers the Examiner to the *Grain Processing Corp. v. American Maize-Products Co.*, case to show that improper hindsight reconstruction has been used in forming the outstanding rejection. 840 F.2d 902, 907, 5 USPQ2d 1788, 1792 (Fed. Cir. 1988) (“Care must be taken to avoid hindsight reconstruction by using ‘the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.’”) (internal citation omitted); *see also In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988), regarding impermissible level of hindsight reconstruction (“One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.”). Applicant is aware some hindsight is allowable. However, an impermissible level of hindsight reconstruction has been used to form the instant rejection.

Thus, Applicant respectfully submits that the Examiner has not presented objective evidence in combining Thorns ‘241 with Zawistowski ‘694, nor has the Examiner met the initial burden of providing the proper suggestion of the desirability of doing what the inventor for this application has done. *Ex parte Clapp*. Further improper hindsight reconstruction has been applied. *In re Vaeck*; *Grain Processing Corp.*; *In re Fine*.

Summary

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Art Unit 1645
Reply to Office Action of December 2, 2004

Therefore, a *prima facie* case of obviousness has not been established since the requirements thereof have not been satisfied. Further, an impermissible level of hindsight reconstruction has been used to form the instant rejection. Thus, the outstanding rejection is improper and/or overcome. Accordingly, Applicant respectfully requests reconsideration and the withdrawal of this rejection.

Conclusion

A full and complete response has been made to all issues as cited in the Office Action. Applicant has taken substantial steps in efforts to advance prosecution of the present application (e.g., filing an Appeal; addressing the new rejection). Further, Applicant respectfully traverses the reopening of prosecution based on the cited combination of Thorns '241 and Zawistowski '694 since a *prima facie* case of obviousness has not been established as discussed above. Thus, Applicant respectfully requests that a timely Notice of Allowance issue for the present case.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez (Reg. No. 48,501) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

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Art Unit 1645

Reply to Office Action of December 2, 2004

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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